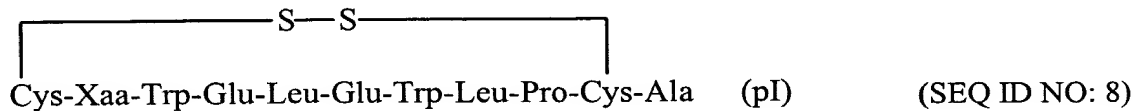


Please substitute the following claim 9 for pending claim 9:

03 9. (Twice amended) A cyclic peptide having the structure:



wherein Xaa is Tyr or Ala.

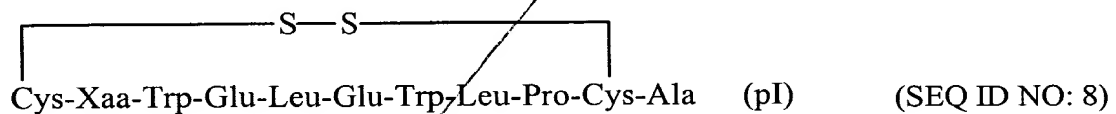
Please substitute the following claim 11 for pending claim 11:

04 11. (Once amended) A peptide of claim 9, wherein Xaa is Tyr (SEQ ID NO:10).

Please add the following new claims:

05 Sub D' 20. (New) A method of identifying or designing a phospholamban deactivator, comprising the steps of:

(a) obtaining a three dimensional structure of a cyclic peptide



wherein Xaa is Tyr or Ala;

(b) creating a three dimensional model of a complex of the cyclic peptide bound to phospholamban cytosolic domain or ligand-binding portion of the phospholamban cytosolic domain thereof;

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Cont.

(c) employing the three dimensional model of the complex to identify a ligand binding site on the phospholamban cytosolic domain or the ligand-binding portion of the phospholamban cytosolic domain thereof, wherein the ligand binding site is the site at which the phospholamban deactivator binds when the phospholamban deactivator is bound to phospholamban;

(d) selecting a candidate molecule that is capable of interacting with the ligand binding site on the phospholamban cytosolic domain or ligand-binding portion of the phospholamban cytosolic domain thereof or that possesses good steric and electrostatic complementarity with the ligand binding site; and

(e) identifying the selected candidate molecule as a potential phospholamban deactivator, wherein the potential phospholamban deactivator can be subsequently synthesized and tested for its ability to function as the phospholamban deactivator.

21. (New) The method of claim 20, which further comprises:

(f) synthesizing the potential phospholamban deactivator and testing the synthesized potential phospholamban deactivator for activation of CaATPase in the presence of phospholamban.

22. (New) The method of claim 20, wherein step (a) comprises obtaining a first set of atom coordinates defining the three dimensional structure of the cyclic peptide.

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D2

23. (New) The method of claim 20, wherein step (b) comprises:

(i) obtaining the first set of atom coordinates defining the three dimensional structure of the cyclic peptide of step (a);

(ii) obtaining a second set of atom coordinates defining the phospholamban cytosolic domain or ligand-binding portion of the phospholamban cytosolic domain thereof; and

(iii) employing a computer-aided molecular modeling program to combine the first set of atom coordinates with the second set of atom coordinates to create a three dimensional model of a complex of the cyclic peptide bound to phospholamban cytosolic domain or ligand-binding portion of the phospholamban cytosolic domain thereof.

24. (New) The method of claim 20, wherein step (c) employs a computer-aided molecular modeling program to identify the ligand binding site on the phospholamban cytosolic domain or the ligand-binding portion of the phospholamban cytosolic domain thereof.

25. (New) The method of claim 20, wherein step (d) employs a computer-aided molecular modeling program to identify the compound capable of interacting with the ligand binding site of the phospholamban cytosolic domain or portion thereof.

26. (New) The method of claim 20, wherein step (d) comprises:

(i') providing atom coordinates defining a three-dimensional structure of the phospholamban cytosolic domain or ligand-binding portion of the phospholamban cytosolic domain thereof that is in a conformation which allows binding of the phospholamban deactivator;

(ii') combining the atom coordinates defining the three-dimensional structure of the phospholamban cytosolic domain or ligand-binding portion of the phospholamban cytosolic domain of step (i') with a set of atom coordinates defining a three dimensional structure of a candidate molecule;

CS  
Cont.  
(iii') employing a computer-aided molecular modeling program, with the atom coordinates defining the three-dimensional structure of the phospholamban cytosolic domain or ligand-binding portion of the phospholamban cytosolic domain and the atom coordinates defining the three dimensional structure of the candidate molecule, to evaluate the ability of the candidate molecule to interact with the ligand binding site of the phospholamban cytosolic domain or ligand-binding portion of the phospholamban cytosolic domain thereof; and

(iv') selecting the candidate molecule that interacts favorably with the ligand binding site of the phospholamban cytosolic domain or ligand-binding portion of the phospholamban cytosolic domain thereof, or that possesses good steric and electrostatic complementarity with the ligand binding site.

27. (New) The method of claim 26, wherein the atom coordinates defining the three-dimensional structure of the phospholamban cytosolic domain or ligand-binding portion of the phospholamban cytosolic domain thereof are derived from the three dimensional model of the complex created in step (b).

28. (New) The method of claim 26, wherein step (iii') comprises:

(iiia') performing a fitting operation between the candidate molecule and the ligand binding site of the phospholamban cytosolic domain or ligand-binding portion of the phospholamban cytosolic domain thereof; and

(iiib') analyzing the results of the fitting operation to quantify association between the candidate molecule and the ligand binding site of the phospholamban cytosolic domain or ligand-binding portion of the phospholamban cytosolic domain thereof.

29. (New) The method of claim 26, wherein step (iii') comprises:

(iiia'') displaying in a graphical format a protein structure encoded by the combination of the atom coordinates defining the three-dimensional structure of the phospholamban cytosolic domain or ligand-binding portion of the phospholamban cytosolic domain and the atom coordinates defining the three dimensional structure of the candidate molecule; and

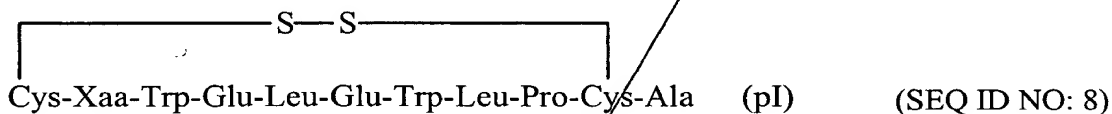
(iiib'') visually inspecting the protein structure displayed in the graphical format to evaluate the ability of the candidate molecule to interact with the ligand binding site of the phospholamban cytosolic domain or ligand-binding portion of the phospholamban cytosolic domain thereof.

30. (New) The method of claim 20, wherein Xaa of the cyclic peptide is Tyr (SEQ

ID NO:10).

31. (New) A method of identifying a target area on the surface of phospholamban, comprising the steps of:

- (a) obtaining a three dimensional structure of a cyclic peptide



wherein Xaa is Tyr or Ala;

- (b) creating a three dimensional model of a complex of the cyclic peptide bound to phospholamban cytosolic domain or ligand-binding portion of the phospholamban cytosolic domain thereof; and

(c) employing a computer-aided molecular modeling program and the three dimensional model of the complex to identify the target area on the surface of phospholamban, wherein said target area is the site at which a phospholamban deactivator binds when said phospholamban deactivator is bound to phospholamban.

32. (New) The method of claim 31, wherein Xaa of the cyclic peptide is Tyr (SEQ ID NO:10).

33. (New) A method of preventing inhibition exerted by phospholamban on CaATPase in a cardiac cell, comprising introducing the cyclic peptide of claim 9 into a cardiac cell.